

Lung isolation, one-lung ventilation and hypoxaemia during lung isolation

Address for correspondence:

Dr. Atul Purohit,
C-26, Mukherji Colony, Shastri
Nagar, Jaipur - 302 016,
Rajasthan, India.
E-mail: apurohit66@yahoo.com

Atul Purohit, Suresh Bhargava¹, Vandana Mangal², Vinod Kumar Parashar

Department of Anaesthesiology, SIDSS, Santokba Durlabhji Memorial Hospital, ¹Department of Anesthesia and Critical Care, Mahatma Gandhi Medical College, ²Department of Anesthesia, SMS Medical College, Jaipur, Rajasthan, India

ABSTRACT

Lung isolation is being used more frequently in both adult and paediatric age groups due to increasing incidence of thoracoscopy and video-assisted thoracoscopic surgery in these patients. Various indications for lung isolation and one-lung ventilation include surgical and non-surgical reasons. Isolation can be achieved by double-lumen endotracheal tubes or bronchial blocker. Different issues arise in prone and semi-prone position. The management of hypoxia with lung isolation is a stepwise drill of adding inhaled oxygen, adding positive end-expiratory pressure to ventilated lung and continuous positive airway pressure to non-ventilated side.

Key words: Hypoxia, lung isolation, one-lung ventilation, shunt fraction, techniques

Access this article online
Website: www.ijaweb.org
DOI: 10.4103/0019-5049.165855
Quick response code


INTRODUCTION

The two lungs on each side of the thoracic cavity are two separate organs morphologically, but act as one functional unit, inflating and deflating in unison to maintain the normal levels of oxygen and CO₂ in the blood. However, situations arise when separation of these two from each other becomes desirable for retrieving, retaining or maintaining healthy, normal functioning of the body. This separation of two lungs, termed as 'lung isolation', makes each of them function as an independent unit and is achieved by preparation of the airway through proper manipulation and instrumentation. This provides improved exposure of the surgical field, and protection of healthy lung from infected or bleeding one. However, on the flip side of it, one-lung ventilation (OLV) also causes more manipulation of airway, and hence more damage, and leads to significant physiological derangements such as ventilation-perfusion mismatching and early development of hypoxia.

The present review aims at making the learning and practicing anaesthesiologist familiar with the method of isolating lungs in both adults and paediatric age groups, the physiological changes that occur during OLV and the methods to prevent and treat hypoxia if it occurs during OLV.

For the purpose of writing a proper review, reference were included from textbooks, journals and online research sources including Medline and PubMed, and all relevant references were included till the latest, 2014.

INDICATIONS OF ONE-LUNG VENTILATION

Surgical procedures

Thoracic surgeries

Related to respiratory system

Lung resection procedures

Bullectomy

Pneumonectomy

Lobectomy

Wedge resection

Video-assisted thoracoscopic surgery (VATS)

Decortication

Diaphragmatic hernia repair (thoracic approach)

Single-lung transplant post-operative complications.

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Purohit A, Bhargava S, Mangal V, Parashar VK. Lung isolation, one-lung ventilation and hypoxaemia during lung isolation. *Indian J Anaesth* 2015;59:606-17.

Related to cardiovascular system

- Minimally invasive cardiac surgeries
 - Valve repairs/replacements
- Aortic arch surgeries
 - Dissecting aneurysm of aortic arch
- Repair of pericardial window
- Pericardiectomy.

Related to esophagus

- Minimally invasive thoraco-laparoscopic oesophagectomy.

Non-thoracic surgeries

- Anterior fixation of the thoracic spine.

Non-surgical indications

- Pulmonary lavage
- Split/differential lung ventilation
- Unilateral lung haemorrhages
- Ventilation in bronchopleural fistulae
- Prevention of spillage from infective to the non-infective lung.

TECHNIQUES OF LUNG SEPARATION

In general, two methods have been used for isolating a lung.

Endobronchial tubes

These are of two types:

- A. Single-lumen endobronchial tubes (EBTs), which are longer than normal endotracheal tubes, but with smaller external diameters and smaller cuffs. These tubes are inserted into a particular main-stem bronchus; ventilate that side lung, causing spontaneous absorption collapse of the other lung. This is a not so commonly used method for lung isolation, and if used, is employed only in small children. An important feature of EBTs is a narrow bronchial cuff and a relatively short distance from the proximal age of that cuff to the distal tip of the tube. Thus, there is a lesser chance of bronchial cuff obstructing the upper lobe bronchus that may occur easily if single-lumen endotracheal tubes (ETTs) are used for this purpose. This 'margin of safety', is defined as the length of the tracheobronchial tree over which a tube can be moved or positioned without obstructing a conducting airway. This is very small with normal ETTs and much larger for EBTs. For emergency situations, normal ETTs can be used, e.g., acute contralateral tension pneumothorax,

acute airway haemorrhages etc., but for all situations double-lumen tubes (DLTs)/bronchial blockers (BBs) are a better choice.

- B. DLTs: By far, the most commonly used method of lung isolation used since they have been introduced, DLTs have been modified in the various base from 1931 till date. DLT's, first used in 1931 by gale and waters^[1] as a cuffed rubber ETT pushed into bronchus of the desired side, have come a long way passing through stages of Carlens catheter^[2] (DLT with hook at carina to ensure correct tube positioning-only left-side), Bryce-Smith tube^[3] (left-side DLT without carinal hook) Robertshaw tubes^[4] (present day red-rubber rigid, fixed curvature DLT), to disposable plastic Broncho-Cath^{®[5]} and next to the Silbroncho tubes^[6] (left-side soft EBT made of silicon rubber with bronchial part wire-reinforced). These have many advantages [Table 1] to offer over the other methods used for lung isolation, such as the ease of insertion and confirmation of position and the ability to isolate, selectively ventilate or collapse either lung independently according to operative requirement.

Endobronchial blockers

These are inflatable balloon-tipped stylets inserted in the desired bronchus to cause blockade of aeration of that particular segment of lung causing collapse, distal to the blocker.^[7-9]

DOUBLE-LUMEN TUBES

All DLTs are essentially two tubes of unequal length, joined together side by side to form one single unit. The two are separated at their proximal end to facilitate independent connection to separate breathing circuits, or to the same circuit through a Y-connector. At the distal end, the shorter tube ends to lie in mid-trachea and the longer tube more distally into the main-stem bronchus of the desired side, to which the DLT is ascribed. All DLTs are curved in two planes. The main-stem which lies in the trachea is concave anteriorly while the more distal bronchial portion is curved at right angle to this

Table 1: Advantages and disadvantages of DLT

Advantages	Disadvantages
Large luminae facilitate suctioning	Difficulties in selecting proper sizes
Best device for absolute lung separation	Difficult to place during laryngoscopy
Conversion from 2 to 1 lung ventilation easy and reliable	Damage to tracheal cuff
	Major tracheobronchial injuries

DLT – Double-lumen tube

with concavity towards the side whose bronchus is to be negotiated (viz., concavity of right-sided DLT bronchial part is towards the right-side). DLTs are side-specific meaning that they are either left-sided or right-sided and the two differ in their structure slightly. Due to the lesser angulation of the right bronchus with the trachea, the right DLT is lesser oblique at its bronchial part than the left. Also, the right DLT has a special opening for right upper lobe (RUL) bronchus, in its bronchial stem, before it ends finally between the points of RUL bronchus' origin and right bronchial carina, a distance of about 2 cm. For this reason, the cuff of right DLT is either obliquely shaped, with RUL bronchial opening incorporated in the slanting cuff in Broncho-Cath® (Mallinckrodt Inc., St. Louis, Missouri, USA) of DLTs, or has two smaller cuffs, the RUL bronchial opening lying between them in Rusch® tubes.

The most commonly used DLT at present are the disposable plastic-cuffed DLTs. These are available in sizes 30, 32, 33, 35, 37, 39 and 41 Fr (both sides) for adults and 26 and 28 (left-side only) for children of 8 to 12 years age. The tracheal and bronchial components of these tubes are color-coded as white and blue, respectively, and have respective cuffs with the same colour. Tracheal cuff, when inflated, allows positive pressure ventilation of both lungs and separation of lungs from the environment, while the inflation of bronchial cuff allows separation of the two lungs from each other. These tubes have a D-shaped lumen in the cross section.

Advantages and disadvantages of double-lumen tubes

These are presented in Table 1.

Method of insertion of double-lumen tubes

As a standard precaution, the DLTs should be checked for their patency, integrity of cuff, the proper

connections including the soft rubber extensions, the Y-connector to the circuit and finally the availability of the clamp used for blocking one side of the tube while checking the correct position. Under direct laryngoscopic vision, the DLT with its stylet in the bronchial lumen is introduced in the oral cavity, with a bronchial concavity facing anteriorly and advanced into the larynx. Once the bronchial cuff is beyond the glottis, at which point the more proximal tracheal cuff would be at the level of incisors, the stylet is removed and the tube rotated by 90° on its long axis towards the side to which it is to be inserted. Further negotiation of the tube can be with either of the following steps. One is to keep pushing the tube blindly till a definite resistance is encountered and pushing beyond which becomes evidently difficult. The tube has most likely reached the desired depth and can be checked by methods described later. The other method, described by Ovassapian,^[10] is inserting a flexible fibre-optic bronchoscope (FOB) into the bronchial lumen, seeing the carina, identifying the 'to be negotiated' bronchus entering this with the FOB and using this FOB as an optical stylet over which the bronchial part of the DLT is threaded.

Confirmation of position of double-lumen tube

This can be achieved by:

1. Sequentially inflating the respective cuffs, blocking the individual components of the DLT (tracheal or bronchial) with a clamp and observing the entry and exit of air through the unblocked component, shown by appearance of water vapour during expiratory phase, observing the unilateral expansion of the chest and finally auscultating the chest for presence or absence of breath sounds or,
2. Using the FOB to see inside both tracheal and bronchial lumina of DLT; when in tracheal lumen, the scope, immediately after coming out of the distal tracheal opening, should show the carina, the blue coloured bronchial stem of DLT entering into the respective bronchus, the inflated blue cuff occupying the entire bronchial lumen and absence of air leak and herniation of bronchial cuff into the other side bronchus across the carina [Figure 1a]. Under fibre-optic vision on right-side with right DLT's bronchial component in the right main bronchus, three openings viz., one proximal for RUL and two distal ones for right bronchial carina should be seen [Figure 1b and c]. On the left-side, only two distal openings of left main

Table 2: Advantages and disadvantages of bronchial blockers

Advantages	Disadvantages
Easy recognition of anatomy if the tip of a single tube is above carina	Small channel for suctioning
Best device for patients with difficult airways	Conversion from 1 to 2 then to 1 lung ventilation (problematic for novice)
No cuff damage during intubation	High maintenance device (dislodgement or loss seal during surgery)
No need to replace a tube if mechanical ventilation is needed	

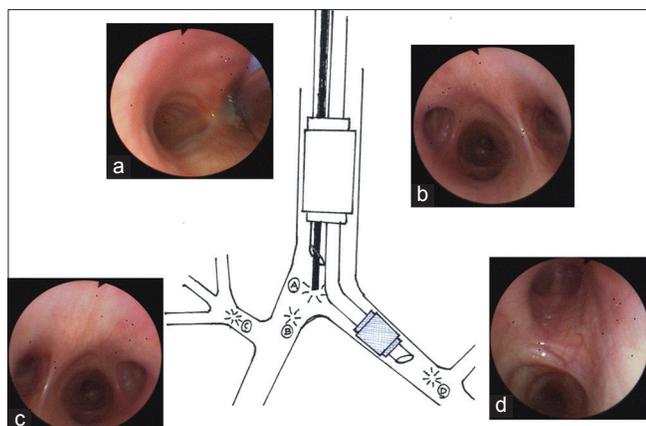


Figure 1: (a-d) Fibre-optic view of tracheal and bronchial carina with left sided double lumen tube *in situ*

bronchial carina would be seen [Figure 1d]^[11,12] as there is no separate opening for left upper lobe bronchus proximally. The second method, that is, use of FOB to directly visualize the position of the DLT has been shown to increase the success rate of DLT insertion, to save time and reduce the complication rate and is strongly recommended.^[13,14]

A recent development in facilitating, confirming the position of DLT and to identify its displacement is the VivaSight-DL® (E.T. view Medical Ltd.,)^[15] This is a left-sided DLT (sizes 37, 39, 41 F only) with a high resolution camera at the tip of the tracheal lumen that remains connected to a monitor and allows continuous visualisation of tracheal carina. Any displacement from the desired position is easily detected and rapid repositioning achieved without disrupting the ventilation. This reduces the need of FOB, offers continuous visualisation of the position of the DLT around the carina^[16] and is also expected to save time in inserting, confirming and repositioning of displaced DLT, once the learning curve is crossed.

Choice of appropriate double-lumen tube

Three criteria need to be looked into. These are:

1. Side selection of DLT: As it is more technical and complicated to insert a right-side DLT due to exact adjustment of RUL branch opening of the bronchus and corresponding orifice in right-side DLT, it is usual to use left-sided DLTs as far as possible for OLV. The main argument against the use of right-side DLT is the relative low margin of safety due to this RUL bronchus anatomy. It entails more frequent displacement and hence more frequent repositioning for right DLTs. The left-sided tube can serve good for

lung isolation, of all situations and there are very limited indications or using right-sided DLT. The right-sided DLTs are required in situations where left main bronchus has been anatomically altered significantly, e.g., due to compression by tumour or thoracic aortic aneurysm, or where surgical procedure involves the left main bronchus, e.g., left main bronchial resection or repair, left pneumonectomy or lung transplantation

2. Size of DLT: The optimal size of DLT for an individual would be the largest tube that passes atraumatically through the glottic opening, advanced down the trachea and fits in the bronchus with a small air leak around the deflated cuff. A DLT too small requires a large cuff volume which could cause endobronchial cuff to herniate and block the other side bronchus, would have a narrower lumen and hence a higher airflow resistance and also pose difficulty in clearing secretions by suctioning. Many methods have been used studied to measure the thickness of bronchus to help estimate the size of DLT to be used. Usually, age, sex and height of the individual have been used to estimate the size of DLT. However, more objective evidence for this was provided by Brodsky *et al.*, who used tracheal diameter measured on chest X-rays to estimate the bronchial size.^[17] They based their estimation on the bronchus-tracheal cross-sectional diameter ratio of 0.68^[18] and concluded that irrespective of age or height, size 41 Fr DLT was appropriate for all male patients. However, no such specification was stated for females. Hannallah *et al.*^[19] measured left bronchial diameter on computed tomography scan. Brodsky *et al.*^[20] also found that tracheal width (TW) was the best predictor of left bronchial width (LBW) and the mathematical equation with normalisation of X-ray magnification, was suggested as: $LBW (mm) = 0.45 \times TW (mm) + 3.3 mm$
3. The depth of insertion of DLT: The tube should be inserted, as stated earlier, to the point where its further insertion faces an evident resistance. This in individuals of either sex, of 170 cm height is attained at 29 cm mark on the DLT. It was estimated by Brodsky, Benumof *et al.*^[21] that for each 10 cm increase or decrease in height, average placement depth was correspondingly increased or decreased by 1 cm. Chow *et al.*^[22]

found that the depth of DLT insertion correlated significantly with the height and Clavicle-to-Carinal (Cl to Car) distance of trachea, with best correlation as: Depth of insertion (cm) = 0.75 × Cl to Car (cm) + 0.112 × ht (cm) + 6.

Complications of double-lumen tubes

1. Malposition – More than 1 cm change in either direction from the desired position of the DLT, as detected by flexible FOB, definitely needs correction.^[13,21,23] It is mandatory now as a standard of care to check with FOB, first after insertion and then after any change of position of the patient, especially from initial supine to final lateral surgical position. Wrongly positioned right-sided DLT will lead to collapse of RUL, if the two openings do not match with each other
2. Airway trauma – Rupture of tracheobronchial tree, or direct trauma to vocal cords causing post-operative hoarseness of voice
3. Others – Stapling of the bronchial lumen of DLT with the bronchus during pneumonectomy.

The DLT needs to be replaced with a single-lumen ETT post-operatively before the patient is shifted to the ICU, if post-operative ventilation is contemplated. This decision involves weighing of risk-benefit ratio by the anaesthesiologist, as changing the tube with a loss of airway control, and regaining it with ETT can be very risky at times; particularly when surgery has lasted long and fluid resuscitation with large amounts could have caused oedema of upper airway. For such occasions, airway exchange catheters (AECs) should be considered, the longer ones especially design for DLTs should be optimal. The AECs serve a dual

purpose, it would act as a guide to the airway and would permit jet ventilation through the central lumen thus preventing hypoxia during airway exchange.

BRONCHIAL BLOCKERS

Besides the DLTs, another method for facilitating lung isolation involves blockade of a bronchus to allow lung collapse distal to the occlusion using devices known as the endobronchial blockers (EBBs). [Figure 3a-f] These include Fogarty's, Foley's and Swan-Ganz catheters, Univent tubes and Torque Control Blocker Univent (TCBU) blockers,^[7] Coopdech blockers, Cohen's tip-deflecting blockers,^[8] Arndt wire-guided endobronchial blockade (WEB) blockers^[9] and the latest EZ-blockers. Table 3 enumerates the advantages and disadvantages of bronchial blockers in general. The salient features of each of these are discussed henceforth in adequate detail.

Fogarty's vascular embolectomy catheter

1. Fogarty's vascular embolectomy catheter® (Edwards Lifesciences, Irvine, CA, USA)^[24] These are balloon-tipped catheters [Figure 3a], similar to the others including Foley's urethral and Swan-Ganz pulmonary arterial catheters with the distal end closed have very efficiently been used for blocking the main-stem or second generation bronchi in both adults and paediatric age groups. The advantages, disadvantages and other salient features are enumerated in Tables 3 and 4.

The Univent tube

This device, introduced by Inoue in 1982,^[7] is a flexible, single-lumen, 'silastic' ETT containing a small

Table 3: Salient features of various bronchial blockers

	Fogarty's catheter	Arndt blocker	Cohen's blocker	Fuji Univent blocker	EZ blocker
Size (Fr)	6-8	5, 7, 9	9	4.5, 9	7
Length (cm)	80	65 and 78	65		
Balloon shape	Spherical 0.5-10 ml capacity	Spherical or elliptical	Spherical	Spherical	Spherical×2
Guidance mechanism	FOB	Nylon wire loop that is coupled with the FOB	Torque device at 55 cm mark to deflect the pre-angled distal tip	None, pre-shaped tip. In TCBU, incorporated torque controlled blocker shaft	None
Method of insertion	Coaxial or parallel	Coaxial; parallel very difficult	Coaxial or parallel	Coaxial or parallel	Coaxial
Smallest recommended SLETT for coaxial use*		5 Fr (4.5 SLETT), 7 Fr (7.0 SLETT), 9 Fr (8.0 SLETT)	9 F (8.0 SLETT)	9 F (8.0 SLETT)	7.5
Murphy's eye		Present in 9 F	Present	Not present	Not present
Centre channel		1.4 mm internal diameter	1.6 mm internal diameter	2.0 mm internal diameter	1.4 mm internal diameter

FOB – Fibre-optic bronchoscope; SLETT – Single-lumen endotracheal tube; TCBU – Torque Control Blocker Univent

additional channel within the concave anterior wall that houses a pre-shaped retractable cuffed bronchial blocker [Figures 2 and 3b] used for lung isolation.^[25]

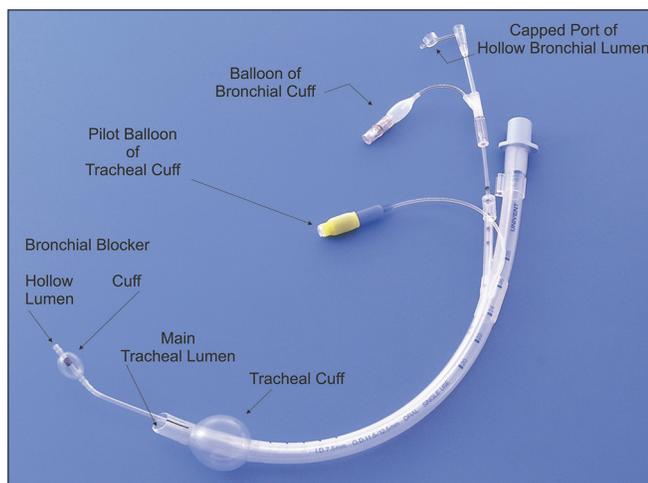


Figure 2: Schematic diagram of the Univent tube with bronchial blocker in position

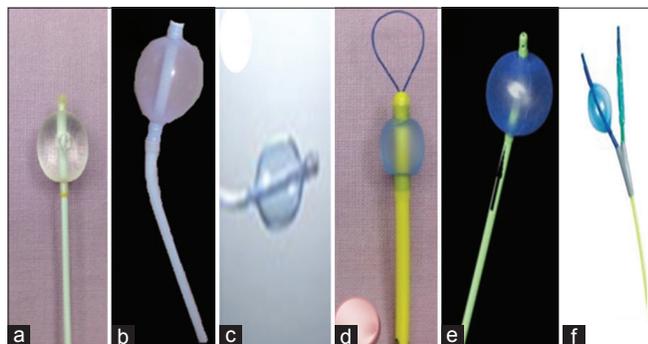


Figure 3: (a-f) Tips of bronchial blockers

When retracted in the tube, this blocker acts as a stylet, angling the tip of the tube for an easier passage into the larynx. The salient features of this tube and the blocker (TCBU[®]) (Vitaid Lewinston, NY, USA) are enumerated in Table 4. The smallest size tube (outer diameter 7.5/5 mm equivalent to 5.5 Fr ETT) can be used in children over 6–8 years of age only.

Advantages of Univent tubes include

1. Being shaped like a conventional single-lumen ET tube, these can be conveniently inserted under direct laryngoscopic vision, for cases of difficult intubation
2. Can be used in fibre-optic intubation in an awake patient
3. Can be used for selective lobar bronchial blockade
4. Can be used as a regular ET tube without the need to change the tube, if post-operative ventilation is contemplated.

Disadvantages in addition to the ones stated in Table 2 include higher bronchial cuff pressures causing injury to the intubated bronchus and costs higher than DLT's.^[26]

Coopdech blocker

2. This 9 Fr, 60 cm long blocker [Figure 3c] is featured with a spindle-shaped or a rectangular, blue coloured high volume low pressure cuff, a Murphy's eye, a central channel and a pre-formed angulated tip. It comes in two types, type 1 without auto inflation mechanism and

Table 4: Tube/bronchial blocker selection for SLV in infants, children and teens

Age (years)	SLETT (1D)	SLETT (1D) micro cuff	Bronchial blocker	Univent	DLT (Fr)
0.5*-1	3.5*-4.0	3.0* micro cuff	5.0* Arndt BB (and WEB) Extra-luminal placement		
1*-2	4.0*-4.5	3.0*-3.5 micro cuff	5.0* WEB extra-luminal placement		
2-4	4.5-5.0	3.5*-4.0 micro cuff	5.0* WEB co-axial or parallel placement		
4-6	5.0-5.5	4.0*-4.5 micro cuff	5.0* WEB co-axial		
6-8	5.5-6.0	5.0*-5.5 micro cuff	5.0* WEB co-axial		
8-10	5.5-6.0 cuff	5.5*-6.0 micro cuff	5.0* WEB co-axial	3.5* 7.5/8.0 OD	26* 8.7 OD
10-12	6.0 cuffed 8.2 OD		5.0* WEB co-axial placement	4.5* 8.5/9.0 OD	26-28* 8.7-9.4 OD
12-14	6.5-7.0 cuffed 8.9-9.6 OD		5.0* WEB co-axial placement	4.5* 8.5/9.0 OD	28-32* 9.4-10.6 OD
14-16	7.0 cuffed 8.6 OD		5.0*-7.0 WEB co-axial placement	6.0* 10.0/11.0 OD	35* 11.7 OD
16-18	7.0-8.0 cuffed 9.6-10.9 OD		7.0*-9.0 WEB coaxial placement	7.0* 11.0/12.0 OD	35*, 37 11.7-12.4 OD

Suggested techniques based on the age of the patient are marked with a * mark. SLV – Single lung ventilation; SLETT – Single-lumen endotracheal tube; WEB – Wire-guided endobronchial blockade; DLT – Double-lumen tube; BB – Bronchial blocker

type 2, with inflation mechanism which is controlled by a switch placed outside near the thumb of working hand of the operator. The blocker after being a place near the tracheal carina is guided further into the desired bronchus under direct FOB vision.

Wire-guided endobronchial blocker (WEB)

Wire-guided endobronchial blocker (Arndt blocker; Cook® Critical Care, Bloomington, IN, USA)^[9] [Figure 3d], after its introducer George Arndt (1994), it is considered an independent blocker and has two peculiar features. One, its tip is not pre-shaped or bent and second that the blocker has a narrow lumen in its centre (1.4 mm diameter) which lodges a plastic guide-wire turned into the shape of a loop at its distal end [Figure 4a]. The calibre of this loop can be changed from external manipulation at the proximal end. This wire loop is made to clinch the FOB and is inserted co-axially with the ET tube and beside the FOB, guiding the blocker to the desired bronchus; hence the name wire-enabled blocker or WEB. The cuff or balloon of the Arndt blocker comes in two shapes, one spherical preferred for the right-sided bronchial blockade, and the other more elongated and elliptically shaped preferably used for the left-sided bronchial blockade.^[24] The adapter for connecting the ETT to the ventilating circuit is also specially designed to allow for uninterrupted ventilation during insertion of the Arndt blocker. This unique Cook's multi-port adapter [Figure 4b] has four port openings. The distal one for connection to the ETT, one proximal one directed at right angle to the tube for connection to the breathing circuit, the one in line with ET tube for FOB and the fourth at an acute angle almost parallel to the FOB port for the Arndt blocker. The blocker can be inserted both co-axially and parallel to the ET tube [Table 3]. The Arndt blockers share all the advantages and disadvantages of bronchial blockers in general [Table 3], but have two additional disadvantages: (1) Once the web-guide or wire loop is removed, it cannot be re-inserted. Therefore, intra-operative repositioning of the blocker is difficult, for which a new blocker assembly has to be used and (2) more frequent malpositions when compared with TCBU.

Cohen tip-deflecting endobronchial blocker

Cohen tip-deflecting endobronchial blocker^[6] [Figure 3e], introduced in 2004 by Cook Critical Care is a 65 mm long catheter shaft with a distal nylon flexible tip which can be deflected approximately 30° in one plane. The FOB and BB can be passed sequentially in the ETT

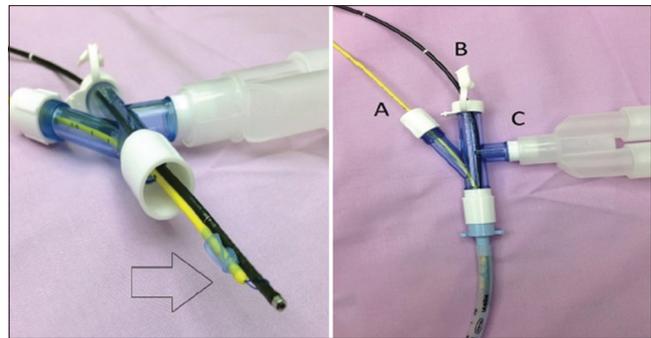


Figure 4: (a and b) Arndt blocker with Cook's multi-port adapter

lumen, FOB following the blocker and the blocker placed *in situ* with lesser resistance. This device can be inserted in 7.5 mm i.d. single-lumen ET tube and hence, is used at best for large teenagers or adults. The manipulation of the tip can be done by a proximal control wheel that can be operated with thumb and index finger of the operator during insertion.

EZ-blocker

EZ-blocker [Figure 3f] is a Y-shaped bronchial blocker with the bifurcation of the main-stem into two distal extensions to be placed in both the main-stem bronchus. The salient features include central lumens of both stems extending into the main shaft and with ports to suck out secretions or to give continuous positive airway pressure (CPAP), radio-opaque shaft, special EZ-multi-port adapter, depth markers on the shaft and two extensions equipped with respective cuffs, each represented proximally by a colour-coded pilot-balloon. These can be inserted co-axially or para-axially, with the aid of FOB. Insertion and removal must be done with the cuffs completely deflated.

LUNG ISOLATION IN CHILDREN

The need for lung isolation in children is increasingly felt with increasing use of thoracoscopy and VATS in paediatric age group. The requirement of a silent lung provides an adequate working space in a relatively small anatomic compartment. In general, the equipment and techniques used for lung isolation in children have been touched upon in previous text; however the tubes or bronchial blockers to be selected for single lung ventilation in infants, children and teenagers have been presented in a tabulated form in Table 4.^[27] The single-lumen tubes, as described earlier are the simplest way of achieving lung isolation in children.^[28] This involves an intentional intubation of one particular bronchus with a thinner than normal conventional ETT until

breath sounds on the operative side disappear. The FOB may be placed para-axially to confirm or guide the placement. The advantages include the simplicity of the method, no requirement of any special equipment except a FOB and the ability to be used as a life-saving procedure in emergency situations such as unilateral lung haemorrhages and contra-lateral tension pneumothorax. However, this method can cause failure to provide adequate seal of the intubated bronchus, especially if a smaller, uncuffed tube is used thus preventing the operated lung from adequately collapsing or failing to protect the ventilated healthy lung from contamination by purulent material in the contra-lateral lung. Inability to suction the operated lung and hypoxia occurring due to obstruction of the more proximally originating upper lobe bronchi, especially on the right-side, are the additional disadvantages of achieving lung isolation with this method. In this regard, the single-lumen endobronchial tubes with smaller bronchial cuffs have a larger ‘margin of safety’^[29] than the uncuffed single-lumen ETTs. Additional methods described in literature for the same purpose include: (1) Extra-luminal or para-axial placement of EBBs preferred for small children due to non-availability of compatible equipment (ET tubes, FOBs, etc.,) for their co-axial placement. (2) Marraro paediatric endotracheal biluminal tube [Figure 5]. An assembly of two uncuffed tubes joined parallel to each other, with a shorter one as the tracheal part and longer on as the bronchial part. This tube has been reported to be safe and effective in children up to 3 years of age.^[30] (3) High-frequency oscillation (HFO) and high-frequency jet ventilation (HFJV) have been used to maintain oxygenation in OLV in children. This is applied to the non-dependent lung, just like CPAP and maintains the operated lung in a slightly distended position. (4) Other methods have also been described in sporadic case reports.^[31-33]

LUNG ISOLATION IN PRONE POSITION

Use of DLT or OLV for VATS or thoracoscopy in prone or semi-prone position has been a matter of debate in various publications. This is due to the fact that while in the supine position for VATS where OLV is essential, it is not so in the prone position. Good surgical exposure can be achieved with single-lumen tube and double-lung ventilation for surgery in posterior mediastinum with the patient in prone.^[34] This is due to the tendency of the structures of anterior mediastinum falling away from the surgical field



Figure 5: Marraro's bilumen paediatric endotracheal tube

under the effect of gravity, making a space for the surgeon to work without the ipsilateral lung being collapsed. This has particularly been tried especially in thoraco-laparoscopic oesophagectomy and dorsal spine discectomy and fixation.^[35] Significant saving of time in preparing the patient for surgeon was achieved when normal single-lumen tube with double-lung ventilation was used, issues of tube displacement, checking and repositioning were avoided and post-operative respiratory functions were found to be better.^[36] However, the potential disadvantage of a single-lumen ETT is that if an emergency conversion to thoracotomy is required, OLV would be facilitated by a DLT *in situ*.^[37] Also, partial inflation of the operated lung due to ventilation in the presence of artificially induced capnothorax interferes with surgeon's vision. The practice at our centre for TLEs (thoraco laparoscopic oesophagectomy) done in the prone position is to use a DLT and continue ventilating both lungs till a lung collapse is asked for by the surgeon or emergency clinical situation warrants it.

ROLE OF ULTRASONOGRAPHY IN LUNG ISOLATION

Once DLT or BB has been positioned, the ultrasonography (USG) of the chest can be used as a convenient tool to confirm the adequacy of lung isolation. With the intercostal approach, an interface between the soft tissue of chest wall and aerated lung is seen as a hyperechoic line, ‘the pleural line’. In ventilated lung, there is a to and fro movement at the pleural line that corresponds to tidal movement of the lung (lung sliding sign). In the non-ventilated lung, there is the absence of lung sliding, whereas in collapsed lung, the pleural line moves with a heartbeat in a pulsatile manner (lung-pulse sign). Lung-pulse is 93% sensitive and 100% specific for identification of

lung collapse. Thus, if lung sliding on one side and lung-pulse on other are seen on USG, an adequate 'functional lung isolation' can be predicted.^[38]

PATHOPHYSIOLOGY OF HYPOXAEMIA DURING ONE-LUNG VENTILATION

Development of hypoxaemia (arterial oxygen saturation <90%) caused by OLV can be explained by following three factors.

Reduction in oxygen stores of the body, poor oxygenation and compromised ventilation

Directly due to the disease process and also the collapse of one-lung, the functional residual capacity and hence the oxygen stores of the body get significantly reduced in a situation of OLV. These as well as effects of anaesthesia and the lateral decubitus position make the patient highly prone to hypoxia. Compression of ventilated, dependent lung by the weight of mediastinum and by abdominal contents after diaphragmatic paralysis further adds to the gravity of atelectasis of the ventilated lung. Increased closure of small airways with old age, reduced elastic recoil and the lateral position lead further to more atelectasis and hence ventilation-perfusion mismatch, finally terminating in hypoxia.

Dissociation of oxygen from haemoglobin

Reduction in the cross-sectional area available for gaseous exchange to almost half due to non-ventilation of one out of two lungs causes a reduction in arterial oxygen partial pressures, increase in CO₂ levels and respiratory acidosis. These physiological changes lead to rapid dissociation of oxygen from haemoglobin (Bohr effect), to enable easier and rapid release of oxygen to the peripheral tissues, as shown by the steep slope of the oxygen-dissociation curve.

Ventilation-perfusion relationship

During OLV, the non-ventilated lung gets perfused, though to a smaller extent than the dependent ventilated lung. This perfusion is a wasted perfusion and hence a shunt, and causes hypoxia. Lesser the shunt fraction, lesser would be the ventilation-perfusion mismatch and lesser the hypoxia. Three factors can contribute to reduction of this shunt fraction during OLV: (1) Surgical compression of blood vessels of operative, non-ventilated, non-dependent lung reduces the circulation of that lung and hence, portion of cardiac output going to it. (2) Gravitational effects shift more blood towards the dependent lung. (3) Hypoxic pulmonary vasoconstriction (HPV). This is a natural

protective reflex that reduces pulmonary blood flow through non-ventilated lung by 40–50% during OLV resulting in moderation of hypoxia.^[39,40] This is a biphasic reaction with early response starting within seconds, reaching a peak at about 15 min followed by a delayed response in 4 h to cause maximal vasoconstriction.^[41-43] It is triggered at alveolar PO₂ of <100 mmHg, the degree of which is proportional to the degree of hypoxia below this level. HPV response can be influenced by various peri-anaesthetic factors; chronic obstructive pulmonary disease (COPD), cirrhosis, sepsis, female sex, exercise, metabolic and respiratory alkalosis, hypocapnia, hypothermia, Trendelenburg position, haemodilution, nitrous oxide and inhalational anaesthetics especially Halothane cause inhibition of HPV response, that is, prevent correction of V/Q mismatch and hence causing more hypoxia during OLV. Systemic hypertension, metabolic acidosis, hypercapnia, hyperthermia, lateral decubitus position and surgical lung retraction, all potentiate HPV response and hence cause lesser hypoxia during OLV.

MANAGEMENT OF HYPOXIA DURING ONE-LUNG VENTILATION

The incidence of hypoxia during one-lung ventilation (SpO₂ of <90%) is about 5%.^[44,45] This can be predicted, prevented and treated by adopting stepwise maneuvers.

Predicting hypoxemia during one-lung ventilation

A number of factors may predict the possibility of hypoxia during OLV. However, none of these could alone be able to predict the same, as hypoxia is due to play of multiple factors acting at the same time, and influencing each other and the lung physiology, *per se*.

^[44-46]

Low PaO₂ prior to OLV

Left-sided ventilation (due to the smaller size of left lung). A difference of 110 mmHg (280 vs. 170 mmHg) was found in PaO₂ when right and left lungs were ventilated with 100% oxygen during OLV in a study by Schwarzkopf *et al*.^[47] Higher forced expiratory volume in 1 s (FEV1).^[48] This is seen in patients with obstructive lung disease and an inverse correlation exists between the FEV1 and the PaO₂. This can be explained by the development of auto-positive end-expiratory pressure (PEEP) in pts with COPD due to air-trapping, thus reducing atelectasis and hence improving oxygenation.

Also, air trapped in the non-ventilated lung tends to delay the onset of desaturation and hence hypoxia^[49]

Distribution of perfusion: The shunt fraction is determined at least partly by the portion of cardiac output going to the non-ventilated, diseased lung. The lesser this lung gets, the more goes to the healthy, ventilated lung and the higher stays the PaO₂. The availability of lung-perfusion scan can, therefore, indicate the probability of patient getting hypoxic during OLV.^[50] With the same reasoning, the large central parenchymal tumours that are relatively less perfused would pose the patient to hypoxia much lesser than the multiple smaller and peripheral metastatic lesions to be resected.

Prevention and treatment of hypoxemia during one-lung ventilation

Improve pre-operative lung function: The standard five pronged attack is used for pre-operative improvement. It includes reducing irritant exposure including smoking, bronchodilators for airway dilatation, mucolytic agent administration, chest physio-therapy to remove secretions and antibiotics to treat infection if present.

Traditionally, anaesthesiologists aim to attain a maximum possible SpO₂ so that an adequate margin of safety is available in case of emergency. In OLV, such margin can be achieved only with increasing FiO₂ to 100%. However, this FiO₂ is liable to itself cause problems like hyperoxia, absorption collapse of alveoli, etc.,. It may be more prudent to tolerate SpO₂ of 88% as the lowest value rather than aim for 100% SpO₂ with high FiO₂. Such a situation of prolonged desaturation, however, can be detrimental and needs a predetermined drill to manage the situation if it arises. The stepwise action plan is described henceforth in the following text:

1. Assess position of DLT/BB-use FOB preferably^[29]
2. Clear airway of mucous secretions or blood in ventilated lung
3. Increase PEEP up to 10 cm of water to ventilated lung. Higher PEEPs can cause diversion of blood from ventilated to non-ventilated side^[51,52] increasing the shunt and worsening hypoxia. 10 cm of PEEP improves the FRC of dependent lung
4. Increase FiO₂, if lesser is being used, to 100% now
5. CPAP or HFO or HFJV to non-ventilated side.^[52]

This is acceptable only in open thoracotomies and not in VATS and thoracoscopic lung resections as this inflation of lung interferes with vision of surgeon and is usually discouraged

6. Intermittent lung recruitment maneuvers^[52] can be used on operated side of lung
7. Suction catheter connected to auxiliary O₂ port can be inserted in lumen of non-ventilated lung airway this prevents hypoxia without inflating the lung
8. Optimisation of Hb levels and cardiac output
9. If a pneumonectomy is planned, early clamping of pulmonary artery of non-ventilated lung eliminates the entire shunt, thus alleviating hypoxia
10. At times, an intermittent double-lung ventilation technique may have to be resorted to, if nothing else works.

Modulation of perfusion by pharmacological interventions such as administration of nitric oxide and almitrine.^[53,54]

Type of anaesthesia: TIVA versus inhalational anaesthesia-clinically insignificant differences on oxygenation with either of these.^[55-57]

CONTROVERSIES IN LUNG ISOLATION

Lung isolation has been in use for long now, but in the absence of specific and clear guidelines, most of the issues discussed in the text still remain controversial. These include the choice of tube size, method of isolation chosen (SLETT/DLT/BB), unequivocal method of insertion and confirmation of correct placement (blind, clinical or under FOB vision), optimum FiO₂ before and during OLV and the limits of acceptable degree of desaturation, just to name of few. There are choices available, each with its advantages and disadvantages, hence, the controversy continues!

WHAT TO USE AND WHEN

As discussed above, no one single method of lung isolation can be labelled to be the best. The use depends upon the situation and has to be decided on 'as and when' basis. However, Alsharani and Eldawlaty described an algorithm for this in 2014.^[58] This can at best be considered as a guide, but the decision lies with the clinician at the head end of the operation table.

SUMMARY

Since the advent of OLV, the anaesthetic and surgical techniques have come a long way. The safety has increased and complications reduced manifold, as a result of improvement in technique and equipment. Also, lung isolation is now being used in more difficult, uncommon and versatile situations, hence presenting new paradigms for surgeons to explore new horizons with their skill. Development with the same pace is surely going to present the future anaesthesia colleagues with more challenges for their patients, and for themselves.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Gale JW, Waters RM. Closed endobronchial anesthesia in thoracic surgery. *J Thorac Surg* 1931;1:432-7.
- Carlens E. A new flexible double-lumen catheter for bronchspirometry. *J Thorac Surg* 1949;18:742-6.
- Bryce-Smith R, Salt R. A right-sided double lumen tube. *Br J Anaesth* 1960;32:230-1.
- Robertshaw FL. Low resistance double-lumen endobronchial tubes. *Br J Anaesth* 1962;34:576-9.
- Burton NA, Watson DC, Brodsky JB, Mark JB. Advantages of a new polyvinyl chloride double-lumen tube in thoracic surgery. *Ann Thorac Surg* 1983;36:78-84.
- Lohser J, Brodsky JB. Silbronco double-lumen tube. *J Cardiothorac Vasc Anesth* 2006;20:129-31.
- Inoue H, Shohtsu A, Ogawa J, Koide S, Kawada S. Endotracheal tube with movable blocker to prevent aspiration of intratracheal bleeding. *Ann Thorac Surg* 1984;37:497-9.
- Cohen E. The Cohen flexitip endobronchial blocker: An alternative to a double lumen tube. *Anesth Analg* 2005;101:1877-9.
- Arndt GA, Buchika S, Kranner PW, DeLessio ST. Wire-guided endobronchial blockade in a patient with a limited mouth opening. *Can J Anaesth* 1999;46:87-9.
- Ovassapian A. Fiberoptic bronchoscope and double-lumen tracheal tubes. *Anaesthesia* 1983;38:1104.
- Watson CB. Fiberoptic bronchoscopy in thoracic anesthesia. In: Cohen ED, editor. *Textbook of Thoracic Anesthesia*. Philadelphia PA: Springer-Verlog; 2004. p. 1.
- Slinger PD. Fiberoptic bronchoscopic positioning of double-lumen tubes. *J Cardiothorac Anesth* 1989;3:486-96.
- Klein U, Karzai W, Bloos F, Wohlfarth M, Gottschall R, Fritz H, et al. Role of fiberoptic bronchoscopy in conjunction with the use of double-lumen tubes for thoracic anesthesia: A prospective study. *Anesthesiology* 1998;88:346-50.
- Campos JH. Current techniques for perioperative lung isolation in adults. *Anesthesiology* 2002;97:1295-301.
- Popescu WM. Advances in lung isolation techniques, *Anesthesiologynews.com*; 2014. Available form: http://www.anesthesiologynews.com/download/Lung_ANGAM2014_WM.pdf. [Last accessed on 2015 May 22].
- Heir JS, Purugganan R, Jackson TA, Norman PH, Cata JP, Kosturakis A, et al. A retrospective evaluation of the use of video-capable double-lumen endotracheal tubes in thoracic surgery. *J Cardiothorac Vasc Anesth* 2014;28:882-4.
- Brodsky JB, Macario A, Mark JB. Tracheal diameter predicts double-lumen tube size: A method for selecting left double-lumen tubes. *Anesth Analg* 1996;82:861-4.
- Jeseph JE, Merendino KA. Dimensional interrelationships of the major components of the human tracheobronchial tree. *Surg Gynecol Obstet* 1957;105:210-4.
- Hannallah M, Benumof JL, Silverman PM, Kelly LC, Lea D. Evaluation of an approach to choosing a left double-lumen tube size based on chest computed tomographic scan measurement of left mainstem bronchial diameter. *J Cardiothorac Vasc Anesth* 1997;11:168-71.
- Brodsky JB, Benumof JL, Ehrenwerth J, Ozaki GT. Depth of placement of left double-lumen endobronchial tubes. *Anesth Analg* 1991;73:570-2.
- Benumof JL, Partridge BL, Salvatierra C, Keating J. Margin of safety in positioning modern double-lumen endotracheal tubes. *Anesthesiology* 1987;67:729-38.
- Chow MY, Goh MH, Ti LK. Predicting the depth of insertion of left-sided double-lumen endobronchial tubes. *J Cardiothorac Vasc Anesth* 2002;16:456-8.
- Brodsky JB, Lemmens HJ. Left double-lumen tubes: Clinical experience with 1,170 patients. *J Cardiothorac Vasc Anesth* 2003;17:289-98.
- Ginsberg RJ. New technique for one-lung anesthesia using an endobronchial blocker. *J Thorac Cardiovasc Surg* 1981;82:542-6.
- Campos JH. An update on bronchial blockers during lung separation techniques in adults. *Anesth Analg* 2003;97:1266-74.
- Mercier FJ, Fischler M. The Univent tube: A substitute to double lumen tubes. *Ann Fr Anesth Reanim* 1994;13:754-8.
- Hammer GB, Fitzmaurice BG, Brodsky JB. Methods for single-lung ventilation in pediatric patients. *Anesth Analg* 1999;89:1426-9.
- Rowe R, Andropoulos D, Heard M, Johnson K, DeCampli W, Idowu O. Anesthetic management of pediatric patients undergoing thoracoscopy. *J Cardiothorac Vasc Anesth* 1994;8:563-6.
- Brodsky JB. Lung separation and the difficult airway. *Br J Anaesth* 2009;103 Suppl 1:i66-75.
- Pawar DK, Marraro GA. One lung ventilation in infants and children: Experience with Marraro double lumen tube. *Paediatr Anaesth* 2005;15:204-8.
- Takahashi M, Horinouchi T, Kato M, Hashimoto Y. Double-access-port endotracheal tube for selective lung ventilation in pediatric patients. *Anesthesiology* 2000;93:308-9.
- Tsujimoto S, Fujiwara S, Tashiro C. How to perform differential lung ventilation in pediatric cases? *Anesthesiology* 1999;91:327.
- Chengod S, Chandrasekharan AP, Manoj P. Selective left bronchial intubation and left-lung isolation in infants and toddlers: Analysis of a new technique. *J Cardiothorac Vasc Anesth* 2005;19:636-41.
- Li NL, Peng WL, Liu CC, Shih CH. Comparison of the short-term postoperative results of prone positioning and lateral decubitus positioning during thoracoscopic esophagectomy. *Wideochir Inne Tech Maloinwazyjne* 2015;10:37-43.
- King AG, Mills TE, Loe WA Jr, Chutkan NB, Revels TS. Video-assisted thoracoscopic surgery in the prone position. *Spine (Phila Pa 1976)* 2000;25:2403-6.
- Cuesta MA, Biere SS, van Berge Henegouwen MI, van der Peet DL. Randomised trial, minimally invasive oesophagectomy versus open oesophagectomy for patients with resectable oesophageal cancer. *J Thorac Dis* 2012;4:462-4.
- Lin J, Kang M, Chen C, Lin R. Thoracoscopic esophageal mobilization during thoracoscopic three stage esophagectomy, A comparison of lateral decubitus v/s semi prone position. *Interact Cardiovasc Thorac Surg* 2013;17:829-34.

38. Parab SY, Divatia JV, Chogle A. A prospective comparative study to evaluate the utility of lung ultrasonography to improve the accuracy of traditional clinical methods to confirm position of left sided double lumen tube in elective thoracic surgeries. *Indian J Anaesth* 2015;59:476-81.
39. Lohser J. Evidence-based management of one-lung ventilation. *Anesthesiol Clin* 2008;26:241-72, v.
40. Lohser J, Ishikawa S. Physiology of lateral decubitus position, open chest and one lung ventilation. In: Slinger P, editor. *Principles of Practice of Anesthesia for Thoracic Surgery*. DOI 10.1007/978-1-4419-0184-2_5, Springer Science; Business Media. 71-80
41. Balanos GM, Talbot NP, Dorrington KL, Robbins PA. Human pulmonary vascular response to 4 h of hypercapnia and hypocapnia measured using Doppler echocardiography. *J Appl Physiol* 2003;94:1543-51.
42. Nagendran J, Stewart K, Hoskinson M, Archer SL. An anesthesiologist's guide to hypoxic pulmonary vasoconstriction: Implications for managing single-lung anesthesia and atelectasis. *Curr Opin Anaesthesiol* 2006;19:34-43.
43. Grichnik KP, Clark JA. Pathophysiology and management of one-lung ventilation. *Thorac Surg Clin* 2005;15:85-103.
44. Karzai W, Schwarzkopf K. Hypoxemia during one-lung ventilation: Prediction, prevention, and treatment. *Anesthesiology* 2009;110:1402-11.
45. Slinger P, Suissa S, Triolet W. Predicting arterial oxygenation during one-lung anaesthesia. *Can J Anaesth* 1992;39:1030-5.
46. Bardoczky GI, Szegedi LL, d'Hollander AA, Moures JM, de Francquen P, Yernault JC. Two-lung and one-lung ventilation in patients with chronic obstructive pulmonary disease: The effects of position and FiO₂. *Anesth Analg* 2000;90:35-41.
47. Schwarzkopf K, Klein U, Schreiber T, Preussetaler NP, Bloos F, Helfritsch H, *et al.* Oxygenation during one-lung ventilation: The effects of inhaled nitric oxide and increasing levels of inspired fraction of oxygen. *Anesth Analg* 2001;92:842-7.
48. Ng A, Swanevelder J. Hypoxemia during one lung anesthesia; continuing education in anesthesia, critical care and pain. *Br J Anesth* 2010;10:117-22.
49. Determann RM, Royakkers A, Wolthuis EK, Vlaar AP, Choi G, Paulus F, *et al.* Ventilation with lower tidal volumes as compared with conventional tidal volumes for patients without acute lung injury: A preventive randomized controlled trial. *Crit Care* 2010;14:R1.
50. Hedenstierna G. Pulmonary perfusion during anesthesia and mechanical ventilation. *Minerva Anesthesiol* 2005;71:319-24.
51. Inomata S, Nishikawa T, Saito S, Kihara S. "Best" PEEP during one-lung ventilation. *Br J Anaesth* 1997;78:754-6.
52. Cinnella G, Grasso S, Natale C, Sollitto F, Cacciapaglia M, Angiolillo M, *et al.* Physiological effects of a lung-recruiting strategy applied during one-lung ventilation. *Acta Anaesthesiol Scand* 2008;52:766-75.
53. Ichinose F, Roberts JD Jr, Zapol WM. Inhaled nitric oxide: A selective pulmonary vasodilator: current uses and therapeutic potential. *Circulation* 2004;109:3106-11.
54. Takasaki M, Oh-Oka T, Saito Y, Kosaka Y. Low dose almitrine bismesylate improves pulmonary gas exchange during canine one-lung hypoxia. *Crit Care Med* 1989;17:661-5.
55. Abe K, Shimizu T, Takashina M, Shiozaki H, Yoshiya I. The effects of propofol, isoflurane, and sevoflurane on oxygenation and shunt fraction during one-lung ventilation. *Anesth Analg* 1998;87:1164-9.
56. Rogers SN, Benumof JL. Halothane and isoflurane do not decrease PaO₂ during one-lung ventilation in intravenously anesthetized patients. *Anesth Analg* 1985;64:946-54.
57. Boldt J, Müller M, Uphus D, Padberg W, Hempelmann G. Cardiorespiratory changes in patients undergoing pulmonary resection using different anesthetic management techniques. *J Cardiothorac Vasc Anesth* 1996;10:854-9.
58. Alsharani H, Eldawlatly A. Lung isolation algorithm: A novel template. *Saudi J Anaesth* 2014;8:447-8.

Author Help: Reference checking facility

The manuscript system (www.journalonweb.com) allows the authors to check and verify the accuracy and style of references. The tool checks the references with PubMed as per a predefined style. Authors are encouraged to use this facility, before submitting articles to the journal.

- The style as well as bibliographic elements should be 100% accurate, to help get the references verified from the system. Even a single spelling error or addition of issue number/month of publication will lead to an error when verifying the reference.
- Example of a correct style
Sheahan P, O'leary G, Lee G, Fitzgibbon J. Cystic cervical metastases: Incidence and diagnosis using fine needle aspiration biopsy. *Otolaryngol Head Neck Surg* 2002;127:294-8.
- Only the references from journals indexed in PubMed will be checked.
- Enter each reference in new line, without a serial number.
- Add up to a maximum of 15 references at a time.
- If the reference is correct for its bibliographic elements and punctuations, it will be shown as CORRECT and a link to the correct article in PubMed will be given.
- If any of the bibliographic elements are missing, incorrect or extra (such as issue number), it will be shown as INCORRECT and link to possible articles in PubMed will be given.